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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,007	09/25/2003	Wendy H. Raskind	UWOTL121680	8123

26389 7590 02/15/2007

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/671,007	RASKIND ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *9-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1203*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on August 14, 2006 is acknowledged. The traversal regards the restriction of Group I from Group III, and is on the ground(s) that the inventions are related, and that the claims have been amended to clarify the invention. The response further argues that a search of Group I would be co-extensive with a search of Group III "as the claims all relate to methods of detecting mutations in a protein kinase C gamma gene," and also notes that Groups I and III share a common classification.

Applicant's arguments have been thoroughly considered but are not found persuasive for the following reasons. While the examiner agrees that both inventions relate to mutations in the protein kinase C gamma gene, the inventions employ different method steps and are aimed at achieving different objectives, such that the inventions are distinct from one another and would require the use of different search terms and strategies to identify the most relevant art to each. More particularly, a search of Group I requires not only a search for references teaching the methods steps of claim 1, but also a search of SEQ ID NO: 3 (as set forth in claims 7-8), which is not encompassed by the claims of Group III. In contrast, the claims of Group III do not refer to SEQ ID NO: 3, but rather requires a search for particular amino acid sequence alterations that are not set forth in the claims of Group I. Thus, the searches required for each of Group I and Group III are clearly different from one another, and a search of more than one of these inventions would impose a serious burden.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of the species of the H101Y mutation in the reply of November 22, 2006 is also noted. However, as discussed above, the restriction requirement has been made final, such that Group III has not been examined, and the species election is moot.

2. Claims 9-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement with regard to the restriction of Group I from Group III in the reply filed on August 14, 2006.

Specification

3. The use of the trademarks GENBANK, BIGDYE, AMPLICYCLE, and SEQUENCHER has been noted in this application. The trademarks should be capitalized wherever they appear.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Claims 1-8 are drawn to methods "of identifying genetic mutations that are associated with ataxic neurological disease in a mammalian subject" that comprise "identifying a difference between a first nucleic acid sequence of a protein kinase C gamma gene from a first mammalian subject exhibiting ataxia and a second nucleic acid sequence of a protein kinase C gamma gene from a second mammalian subject which is not exhibiting ataxia, wherein the first and second mammalian subjects are members of the same species, and wherein the difference between the nucleic acid sequences represents a genetic mutation in the first nucleic acid sequence that is associated with ataxic neurological disease." Thus, the claims are drawn to methods in which any mutation in the protein kinase C gamma gene of any mammal "exhibiting ataxia" is considered to be "associated with ataxic neurological disease."

It is unpredictable as to whether one of skill in the art could practice the invention of the instant claims. It is noted that the specification does disclose, e.g., a particular mutation, the "C to T transition in nucleotide 301 (H101Y)," that was identified by screening the protein kinase C gamma gene in healthy and diseased populations of human subjects, and which is clearly associated with a particular type of ataxia (the "unexplained cerebellar ataxia" discussed in Example 1) in a particular type of subject (humans), such that one of skill in the art could clearly practice methods of, e.g., diagnosing predisposition to this type of ataxia in a human subject by detecting the presence of this particular alteration in the protein kinase C gamma gene of the human subject. However, the instant claims are not drawn to such methods, but rather are drawn to methods in which the identification of any type of sequence different in any type of mammalian subject exhibiting any type of ataxia (including a single such subject) is considered to constitute the identification of a sequence difference that "represents a genetic mutation....that is associated with ataxic neurological disease." The teachings of the specification are limited to a particular type of subject (humans), and even in this limited case, applicants have reported the presence of many sequence differences with no established association with ataxia (see for example, the list of identified mutations in Table 3, which includes a variety of silent mutations). The specification further teaches that there are many types of ataxia (see pages 1-2), and is silent with regard to any protein kinase C gamma sequence differences in non-human mammals that were found to have an association with ataxia. Lacking guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance that might enable

the practice of a claimed invention. However, in the instant case, such further guidance is lacking, as the prior art is silent with regard to methods encompassed by the instant claims, and does not provide any teaching that sequence differences in any type of mammalian protein kinase C gamma gene could be considered to be "associated with ataxic neurological disease." Given the high level of skill of one skilled in the art relevant to the claimed invention, it is clearly within the ability of such an artisan to conduct screening methods, e.g., employing samples from other types of mammals and/or patients with other types of ataxia so as to determine whether other mutations associated with ataxia exist in the protein kinase C gene of such subjects. However, the outcome of such experimentation cannot be predicted, and further, even if one were to identify a mutation in, e.g., the protein kinase C gamma gene of an ataxic cow as compared to the protein kinase C gamma gene of a healthy cow, one of skill in the art would not simply conclude that such an identified mutation is "associated with ataxia," as directed by the method of the instant claims. Rather, a skilled artisan would recognize that a substantial number of additional steps (for example, a study of larger groups of diseased and healthy animals and statistical analysis of the prevalence of the mutation in the diseased group as compared to the healthy group, etc.) would be necessary before one could conclude that the mutation was "associated with ataxic neurological disease." Further, one skilled in the art would recognize that a mutation indicative of disease in one type of mammal would not necessarily be indicative of disease in other types of mammals, and that a mutation associated with one type of ataxia would not necessarily be associated with another; again, the method steps set

forth in the instant claims would clearly be inadequate to draw conclusions regarding whether any particular mutation is "associated with ataxic neurological disease." Thus, given the lack of guidance in the specification and in the prior art, it would clearly require undue experimentation to use applicant's invention as claimed.

With further regard to claim 3 and claims dependent therefrom, while it is again noted that the specification clearly discloses, e.g., a particular protein kinase C gamma gene mutation that is associated with a particular ataxia type in humans, the instant claims are not drawn to methods that employ such mutations, but rather, are drawn to methods in which any mutation identified in any mammalian protein kinase C gamma gene is treated as being associated with ataxia. While claim 3 does recite a further step of "determining whether the identified genetic mutations cosegregate with ataxia observed in the subjects suffering from ataxia," the claim does not provide any indication as to how this might be done, or indicate how cosegregation might relate to any conclusions drawn regarding ataxia association. The claims as written still encompass treating any protein kinase C gamma mutation identified in any mammal with any type of ataxia as an indicator that the mutation is "associated with ataxic neurological disease."

With further regard to claims 7-8, which recite that the "protein kinase C gamma gene is at least 90%(claim 7)/95%(claim 8) identical" to SEQ ID NO: 3, it is noted that this language further suggests that virtually any difference in the sequence of the protein kinase C gene (including numerous differences existing together, up to 5% or 10% of the gene sequence) would also be treating as "associated with ataxia," and/or

that any difference in a molecule only 90%/95% identical to SEQ ID NO: 3 in an ataxic subject relevant to a non-ataxic subject would be considered as indicative of ataxia. Neither the specification nor the prior art provide evidence of any mutations other than those particular mutations in SEQ ID NO: 3 set forth in applicant's specification that are actually associated with ataxia. Thus, it is further unpredictable as to whether the claimed invention could be practiced with regard to sequences other than SEQ ID NO: 3 itself, and it would clearly require undue experimentation to practice such methods.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are indefinite because it is unclear whether the claims are drawn to methods of "identifying genetic mutations that are associated with ataxic neurological disease," as set forth in the preamble of claim 1, or to methods of identifying a "difference" between nucleic acid sequences that "represents a genetic mutation" that is associated with ataxic neurological disease. More particularly, it is not clear whether the claims require actual identification of a mutation (or mutations, as indicated in the preamble), or whether the claims merely require one to identify some kind of difference in a nucleic acid that "represents" a mutation. It is further unclear what is meant by a difference that "represents" a mutation – what relationships between nucleic acid

molecules and mutations contained therein are encompassed by this terminology? Clarification is required.

Claims 3-6 are indefinite over the recitation of the limitations "the identified genetic mutations" and "the subjects suffering from ataxia" in claim 3 because there is insufficient antecedent basis for these limitations in the claims.

Claims 4-6 are indefinite over the recitation of the limitation "said cosegregation" in claim 4 because there is insufficient antecedent basis for this limitation in the claims. This term is also employed in claims 5-6, which depend from claim 4.

Claim 6 is indefinite over the recitation of the limitation "aberrant restriction enzyme site" because it is unclear what is encompassed by this terminology. For example, is this language intended to refer to, e.g., a difference between a polymorphic and a wild-type molecule that results in one molecule having a site that is present or absent relative to the other molecule, or does the use of the term "aberrant" in some way limit the claim to a particular type or subset of restriction site? A clear definition for this terminology is not provided in either the specification or the prior art, and its meaning is unclear.

Claim 6 is also unclear over the language "cosegregation is determining by the presence of said genetic mutation in a first population....and not present in a second population...." It appears that the phrase "and not present in a second population" may be intended to have the meaning of the language "and absence in a second population....;" however, as the second portion of the phrase does not clearly agree with

or refer back to the first part, the meaning of the recitation "and not present in a second population" is not clear.

Claims 7-8 are indefinite over the recitation of the limitation "the protein kinase C gamma gene" in each of the claims. As claim 1 (from which claims 7-8 depend) recites multiple protein kinase C gamma genes, it is not clear which gene of claim 1 is further limited by the recitation "the protein kinase C gamma gene" in claims 7-8.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634